UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/775,909	02/02/2001	Mark Roberts	M0975/7006 (JRV)	9660

7590 04/27/2005

John R. Van Amsterdam
Wolf, Greenfield & Sacks, P.C.
600 Atlantic Avenue
Boston, MA 02210

EXAMINER	
DUFFY, PATRICIA ANN	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 04/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/775,909	ROBERTS, MARK	
	Examiner	Art Unit	
	Patricia A. Duffy	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9-27-04; 10-13-04; and 1-24-05*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37,39 and 41-55* is/are pending in the application.

4a) Of the above claim(s) *47-54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37,39,41-46 and 55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08/619,600.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO AMENDMENT

The amendment to the claims filed 1-24-05 has been entered into the record. The responses filed 9-27-04 and 1-24-05 have been entered into the record. The unexecuted declaration filed 9-27-04 and the executed declaration filed 10-13-04 have been entered into the record. Claims 37, 39 and 41-55 are pending. Claims 37, 39, 41-45, 46 and 55 are under examination.

The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Election/Restrictions

This application contains claims 47-54 drawn to an invention nonelected without traverse in the response filed 10-7-02. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Rejections Withdrawn

The rejection of claims 37, 39, 41-46 and 55 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is withdrawn in view of the amendment to the claims.

The rejection of claims 37, 39, 41, 43, 44, 46 and 55 under 35 U.S.C. 103(a) as being unpatentable over Wilson et al (Vaccine, 11(2):113-118, 1993; of record) in view of Nenconi et al (Acta Med Rom 29:78-83, 1991; of record) is withdrawn in favor of the reinstated art rejections set forth below as a result of Applicant's amendment to the

claims. The declaration addressing Wilson et al is moot in view of the reinstatement of the previous art rejections of record.

The rejection of claim 42 under 35 U.S.C. 103(a) as being unpatentable over Wilson et al (Vaccine, 11(2):113-118, 1993; of record) and Nenconi et al (Acta Med Rom 29:78-83, 1991; of record) as applied to claims 37, 39, 41, 43, 44, 46 and 55 above and further in view of Capiau et al (EP 352250, published 1-24-90; of record) and Tamura et al (U.S. Patent No. 5,182,109; of record) is withdrawn in favor of the reinstated art rejections set forth below as a result of Applicant's amendment to the claims. The declaration addressing Wilson et al is moot in view of the reinstatement of the previous art rejections of record.

The rejection of claim 45 under 35 U.S.C. 103(a) as being unpatentable over Wilson et al (Vaccine, 11(2):113-118, 1993; of record) and Nenconi et al (Acta Med Rom 29:78-83, 1991; of record) as applied to claims 37, 39, 41, 43, 44, 46 and 55 above and further in view of Halpern et al (Infection and Immunity 58(4):1004-1009, 1990; of record) is withdrawn in favor of the reinstated art rejections set forth below as a result of Applicant's amendment to the claims. The declaration addressing Wilson et al is moot in view of the reinstatement of the previous art rejections of record.

Objection / Rejections Maintained

Claim Objections

Claim 43 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Applicant's arguments have been carefully considered but are not persuasive. Applicant argues that co-administration means that the requirement for "co-administration" allows for the two components to be administered one after the other with a short lag time between administration of the first and second component and points to the last page on 9 that indicates that the components may be administered separately at slightly different times. This is not persuasive, Applicants interpretation is repugnant to the convention meaning of the prefix "co-" which is conventionally defined as "with, together, joint, jointly" (Webster's Ninth New Collegiate Dictionary, 1990, pages 252-253). The specification does not specifically redefine the meaning of "co" to imply something other than "together" or simultaneous. "Together" is defined as "at one time or simultaneously" page 1240 of Webster's Ninth New Collegiate Dictionary. As such, while Applicant indicates that the co-administration is intended to cover proximal or not together/simultaneous, the definition of this term specifically precludes that which Applicants intend it to cover. The term, as being used and interpreted by Applicants is repugnant to its common meaning and has not been specifically redefined in the specification as filed. As such, the objection is maintained for reasons made of record.

New Rejections Based on Amendment

It is noted that the Office Action Mailed 4-18-04 indicated that the rejections over the art of record were withdrawn in view of the specific amendment to the claims. In response to the new matter rejection set forth therein, Applicant has now canceled the new matter and thus the previous art rejections are hereby reinstated as set forth below.

Claims 37, 39, 41-44, 46 and 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over any one of Nencioni et al (Acta. Med. Rom. 29:78-83, 1991) or Podda et al (J. Exp. Med. 172:861-868, 1990) in view of Capiau et al (EP 352250, published 1-24-90), Tamura et al (U.S. Patent No. 5,182,109) and Honda et al (Japanese Application #3-

135923) made of record in the Office Action mailed 12-31-2002, reiterated herein and maintained for reasons made of record in the Final Office Action mailed 7-8-03.

Nencioni et al teaches a double mutant pertussis toxin PT-9K/129G which can be administered alone or in combination with the *Bordetella pertussis* antigens FHA and 69K. (see abstract, page 81, last paragraph, page 82, fifth paragraph).

Podda et al also teach the double mutant pertussis toxin PT-9K/129G which can be combined with the 69 kD protein and FHA. (see especially abstract; page 867, second and last paragraph).

Nencioni et al and Podda et al references differ in not teaching the double mutant toxin and antigen in the form of nasal drops or nasal spray for mucosal administration.

Capiau et al discloses double mutants pertussis toxin S1 subunit with a modification at the tryptophan residue at amino acid position 26 (see especially abstract). Capiau et al also discloses additional modification can be included to produce a double mutant. These modifications include mutations at the glutamic acid at amino acid position 129 or the arginine at the amino acid position 9 (see especially page 6, lines 14-37). In addition, the reference discloses a method of oral or intranasal administration of the mutant pertussis toxin to humans; the toxin can be administered alone or with other antigens such as filamentous haemagglutinin (FHA), tetanus toxoid and/or diphtheria toxoid or any other protective antigen of *Bordetella pertussis*. (see especially page 7, lines 50-56; page 8, lines 41-59).

Tamura et al teach a vaccine preparation comprising a toxin (such as pertussis toxin) combined with a vaccine that can be administered intranasally in the form of a nasal spray or nose drops. The vaccine preparations can be stored in a container until needed. (see abstract, column 9 and column 17). Tamura et al teach that nasal administration has the benefit of stimulating IgA antibody production (see column 3).

Honda et al teach a method of nasal inoculation of pertussis toxin B sub-unit and a vaccine antigen in order to produce an immune response which is greater than

subcutaneous inoculation (see especially abstract, page 1; page 2, last paragraph; page 3, first and fourth paragraph; and page 4, last paragraph).

It would have been prima facie obvious at the time the invention was made to administer the double mutation of Nencioni et al and Podda et al in combination with the *Bordetella pertussis* antigens FHA and 69K by nasal administration because Honda et al teach that nasal inoculation of pertussis toxin and a vaccine antigen produces an immune response which is greater than subcutaneous administration, Tamura et al teaches that nasal administration has the benefit of inducing an IgA response and Capiau et al teach oral or intranasal administration of double mutant pertussis toxins in combination with other antigens such as FHA and such as filamentous haemagglutinin (FHA), tetanus toxoid and/or diphtheria toxoid or any other protective antigen of *Bordetella pertussis* for the protection from disease. The combined teaching so the prior art suggest to one of skill in the art that vaccines comprised of bacterial toxins such as pertussis toxin, can be administered intranasally in the form of nasal drops or nasal sprays in order to produce an greater immune response.

Claim 45 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nencioni et al (Acta. Med. Rom. 29:78-83, 1991) or Podda et al (J. Exp. Med. 172:861-868, 1990); Capiau et al (EP 352250, published 1-24-90), Tamura et al (U.S. Patent No. 5,182,109) and Honda et al (Japanese Application #3-135923) as applied to claims 37-44 and 46 above and further in view of Halpern et al (Infection and Immunity 58(4):1004-1009, 1990) made of record in the Office Action mailed 12-31-2002, reiterated herein and maintained for reasons made of record in the Final Office Action mailed 7-8-03.

Nencioni et al (Acta. Med. Rom. 29:78-83, 1991) or Podda et al (J. Exp. Med. 172:861-868, 1990) in view of Capiau et al (EP 352250, published 1-24-90), Tamura et al (U.S. Patent No. 5,182,109) and Honda et al (Japanese Application #3-135923) as

combined is set forth supra. The method as combined differs in not teaching the combination of the double mutant with fragment C antigen of tetanus toxin.

Halpern et al teach that Fragment C can be a suitable alternative to tetanus toxin in many applications (see especially abstract). Halpern et al also teach that the C fragment antigen retains the activity of the intact tetanus toxin avoiding the need to use the intact tetanus toxin with requires toxioding. Halpern et al also tech a method of immunizing mice with Fragment C to product antibodies.

It would have been prima facie obvious to one of ordinary skill in the art at the time that the invention was made to modify the nasal vaccine as combined by adding Fragment C according to Halpern into the nasal vaccine as combined above and nasally administering the vaccine as so modified because Capiau et al teach that the double mutant pertussis toxin can be combined with tetanus toxoid and Halpern et al teach that Fragment C has the benefits of inducing an appropriate immune response and provides the benefit of not having to make a toxoid of the toxin. One would have been motivated to include Fragment C of Halpern et al to provide additional protection against tetanus while avoiding the use of intact toxins which would require toxoiding.

Status of Claims

Claims 37, 39, 41-45, 46 and 55 stand rejected. Claims 47-54 are withdrawn from consideration as drawn to a noon-elected invention.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-0855. The examiner can generally be reached on M-Th 6:30 am - 6:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patricia A. Duffy

Primary Examiner

Art Unit 1645